

REMARKS

The Specification has been amended to include sequence identification numbers which were omitted at the time of filing.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made.".


The undersigned hereby states that the computer readable form copy (CRF copy) of the Sequence Listing, the compact disk copy (COPY 1) and the duplicate compact disk copy (COPY 2) of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.825(a) and (b), respectively, are the same and contain no new matter. Accordingly, entry of the Sequence Listing into the above-captioned case is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 511582005000. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: December 11, 2001

By:


Kawai Lau
Registration No. (44,461)

Morrison & Foerster LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5178
Facsimile: (858) 720-5125

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at page 6, line 35, has been amended as follows:

Figures 4a-b. Sequence alignment of 158P1D7 (SEQ ID NO.:657) with human hypothetical protein FLJ22774, clone KAIA1575 (SEQ ID. NO.:658).

Paragraph beginning at page 7, line 1, has been amended as follows:

Figure 5a. Amino acid sequence alignment of 158P1D7 (SEQ ID NO.:657) with human protein (FLJ227744, SEQ ID. NO. :659).

Paragraph beginning at page 7, line 3, has been amended as follows:

Figure 5b. Amino acid sequence alignment of 158P1D7 (SEQ ID NO.:657) with human protein similar to IGFALS (SEQ ID. NO.:660).

Paragraph beginning at page 27, line 20, has been amended as follows:

In an embodiment described in the examples that follow, 158P1D7 can be conveniently expressed in cells (such as 293T cells) transfected with a commercially available expression vector such as a CMV-driven expression vector encoding 158P1D7 with a C-terminal 6XHis (SEQ ID NO.:698) and MYC tag (pcDNA3.1/mycHIS, Invitrogen or Tag5, GenHunter Corporation, Nashville TN). The Tag5 vector provides an IgGK secretion signal that can be used to facilitate the production of a secreted 158P1D7 protein in transfected cells. The secreted HIS-tagged 158P1D7 in the culture media can be purified, e.g., using a nickel column using standard techniques.

Paragraph beginning at page 63, line 20, has been amended as follows:

Single chain antibodies comprise the variable domains of the heavy and light chain joined by a flexible linker polypeptide, and are expressed as a single polypeptide. Optionally, single chain antibodies are expressed as a single chain variable region fragment joined to the light chain constant region. Well-known intracellular trafficking signals are engineered into recombinant polynucleotide vectors encoding such single chain antibodies in order to precisely target the intrabody to the desired intracellular compartment. For example, intrabodies targeted to the

endoplasmic reticulum (ER) are engineered to incorporate a leader peptide and, optionally, a C-terminal ER retention signal, such as the KDEL (SEQ ID NO.:699) amino acid motif. Intrabodies intended to exert activity in the nucleus are engineered to include a nuclear localization signal. Lipid moieties are joined to intrabodies in order to tether the intrabody to the cytosolic side of the plasma membrane. Intrabodies can also be targeted to exert function in the cytosol. For example, cytosolic intrabodies are used to sequester factors within the cytosol, thereby preventing them from being transported to their natural cellular destination.

Paragraph beginning at page 72, line 2, has been amended as follows:

pGEX Constructs: To generate recombinant 158P1D7 proteins in bacteria that are fused to the Glutathione S-transferase (GST) protein, all or parts of the 158P1D7 cDNA protein coding sequence are fused to the GST gene by cloning into pGEX-6P-1 or any other GST- fusion vector of the pGEX family (Amersham Pharmacia Biotech, Piscataway, NJ). These constructs allow controlled expression of recombinant 158P1D7 protein sequences with GST fused at the amino-terminus and a six histidine epitope (6X His) (SEQ ID NO.:698) at the carboxyl-terminus. The GST and 6X His tags permit purification of the recombinant fusion protein from induced bacteria with the appropriate affinity matrix and allow recognition of the fusion protein with anti-GST and His antibodies. The 6X His tag is generated by adding 6 histidine codons to the cloning primer at the 3' end of the open reading frame (ORF). A proteolytic cleavage site, such as the PreScissionTM recognition site in pGEX-6P-1, may be employed such that it permits cleavage of the GST tag from 158P1D7-related protein. The ampicillin resistance gene and pBR322 origin permits selection and maintenance of the pGEX plasmids in E. coli. For example, constructs are made utilizing pGEX-6P-1 such that the following regions of 158P1D7 are expressed as an amino-terminal fusions to GST: amino acids 1 to 841; or any 8, 9, 10, 11, 12,13, 14,15, or more contiguous amino acids from 158P1D7 or analogs thereof.

Paragraph beginning at page 75, line 31, has been amended as follows:

Additional pSR α constructs are made that fuse an epitope tag such as the FLAG tag to the C-terminus of 158P1D7 sequences to allow detection using anti-epitope tag antibodies. For example, the FLAG sequence 5' gat tac aag gat gac gac gat aag 3' (SEQ ID NO.:700) is added to cloning primer at the 3' end of the ORF. Additional pSR α constructs are made to produce both N-

terminal and C-terminal GFP and myc/6 HIS fusion proteins of the full-length 158P1D7 proteins. The following regions of 158P1D7 are expressed in such constructs, amino acids 1 to 841; or any 8, 9, 10, 11, 12,13, 14,15, or more contiguous amino acids from 158P1D7, variants, or analogs thereof.

Please replace Table XIX, beginning at page 150, with the following rewritten Table XIX:

Table XIX: Motif-bearing Subsequences of the 158P1D7 Protein	
Protein Motifs of 158P1D7	
N-glycosylation site	
Number of matches: 3	
1	292-295 NDSR (SEQ ID NO.:673)
2	409-412 NLTR (SEQ ID NO.:674)
3	741-744 NQST (SEQ ID NO.:675)
cAMP- and cGMP-dependent protein kinase phosphorylation site	
	262-265 KKES (SEQ ID NO.:676)
Protein kinase C phosphorylation site	
Number of matches: 3	
1	26-28 SSR
2	297-299 STK
3	670-672 TER
Casein kinase II phosphorylation site	
Number of matches: 12	
1	149-152 TVIE (SEQ ID NO.:677)
2	186-189 THLD (SEQ ID NO.:678)
3	231-234 TWLE (SEQ ID NO.:679)
4	290-293 SIND (SEQ ID NO.:680)
5	354-357 SLSD (SEQ ID NO.:681)
6	510-513 TQID (SEQ ID NO.:682)
7	539-542 TVTD (SEQ ID NO.:683)
8	600-603 SLTD (SEQ ID NO.:684)
9	676-679 SLYE (SEQ ID NO.:685)
10	720-723 SLLE (SEQ ID NO.:686)
11	748-751 SFQD (SEQ ID NO.:687)
12	816-819 TKNE (SEQ ID NO.:688)
Tyrosine kinase phosphorylation site	
	798-805 KLMETLMY (SEQ ID NO.:689)
N-myristoylation site	
Number of matches: 8	
1	29-34 GSCDSL (SEQ ID NO.:690)
2	86-91 GLTNAI (SEQ ID NO.:691)
3	106-111 GAFNGL (SEQ ID NO.:692)

4	255-260	GSILSR	(SEQ ID NO.:693)
5	405-410	GSFMNL	(SEQ ID NO.:694)
6	420-425	GNHLTK	(SEQ ID NO.:695)
7	429-434	GMFLGL	(SEQ ID NO.:696)
8	481-486	GVPLTK	(SEQ ID NO.:697)

Two Protein Motifs were predicted by Pfam

1-Archaeal-ATPase at aa 441-451

2-Leucine rich repeat C-terminal at aa 218-268 and aa 517-567